U.S. Food and Drug Administration
Center for Drug Evaluation and Research

Submitting Archival Files

To the CDER

Electronic Document Room

Electronic
Document
Room

Lessons Learned!

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CDER

April 30, 1998

U.S. Food and Drug Administration
Center for Drug Evaluation and Research

Lessons Learned to Speed Processing

Electronic Document Room

- ***27 e-subs of CRTs/CRFs to replace paper***
- ***Over 4.3 million pages***
- ***10,000 Volumes***
- ***1,000 boxes of paper***

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NDA Copies

Electronic
Document
Room

Guidance - Page 1

I. INTRODUCTION

Traditionally, the FDA has required that regulatory submissions, such as investigational new drug (IND) applications and new drug applications (NDAs), be submitted as paper documents. Regulations in 21 CFR Part 314 provide the requirements and procedures for submitting applications to the Center for Drug Evaluation and Research (CDER) to obtain approval for the marketing of new drugs. Among other things, the regulations require the submission of three copies of an application for marketing approval: (1) a complete archival copy, (2) a review copy, and (3) a field copy (21 CFR 314.50(k)).

Two Electronic Submission Types

Electronic Document Room

1. Electronic Archival Files

Designed to Replace paper

Submit with Archival Copy

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2. Review Aids

Designed to Assist Review

Submit with Review Copies

Amendments and Supplements

Electronic Document Room

1. *All materials submitted after initial submission are <u>amendments</u> or <u>supplements</u>*

2. *Each original, amendment or supplement is self-contained w/ it's own Table of Contents*

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Preparation for the CDER Network

Electronic
Document
Room

1. *Follow the Guidance directory structure*
2. *Prepare Table of Contents as described*

The Transport Media

Electronic
Document
Room

Submitted disks and CD-ROMs are the transport media.

Multiple disks will be loaded into one network share

The entire electronic submission will be archived onto 1 DLT tape

Preparing Archive Files

Electronic Document Room

- ***Physical Preparation***
  - *Place E-media in their own standard blue binder*
  - *Label Binder & Disks*
  - *Include cover letter*
  - *Helpful: descriptive info*

Preparing Review Aids

Electronic Document Room

- ***Place review aids with desktop copies***
- ***Place in Separate Appropriate Colored Binders***
- ***Label Binders & Disks***
- ***Include Technical Description & Documentation***

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Shipping Files
Initial Application

Electronic
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The entire Initial submission should be shipped to the CDER Central Document Room (CDR) including all paper & both electronic-media Archival files and review aids.

The CDR is prepared to accept, process & distribute all electronic media.

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Shipping Files
Initial Application

Electronic
Document
Room

Send to:

FDA Center for Drug Evaluation and Research,

Central Document Room

12229 Wilkins Ave.

Rockville, Md. 20852-1833

U.S. Food and Drug Administration
Center for Drug Evaluation and Research

Amendments & Supplements

Electronic Document Room

All Subsequent Submissions:

- ***Paper & review aids***

  Ship to: Division Document Room

In all cases:

- ***Electronic Archive Files***

  Ship to: Central Document Room

Size & Media

Electronic Document Room

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Whenever possible, applicants should choose media capable of holding the submission on the fewest number of units.

Size	*Recommended Media*	*Recommended Max. Units*
! Less than 10MB	*3.5 inch DOS Formatted Floppy Disks*	*1 - 10 Disks*
! Less than 3.25GB	*ISO 9660*	*1 - 5 CDS*
! Greater than 3.25GB	*Digital Equipment Corp. DLT 20/40 and 10/20 GB format (exabyte 8mm format) using OPENVMS with VMS backup or NT server 4.0 with NT backup or backup exec.*	*1 or More Tapes*

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Completing the 356h

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE
(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on last page.

FOR FDA USE ONLY
APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
TELEPHONE NO. *(Include Area Code)*	FACSIMILE (FAX) Number *(Include Area Code)*
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	CODE NAME *(If any)*

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:

(PROPOSED) INDICATION(S) FOR USE:

APPLICATION INFORMATION

APPLICATION TYPE (check one) ☐ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b) (1) ☐ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug Holder of Approved Application

TYPE OF SUBMISSION (check one) ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION

PROPOSED MARKETING STATUS (check one) ☐ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED _____ THIS APPLICATION IS ☐ PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing)

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Completing the 356h

	This application contains the following items: *(Check all that apply)*	
X	1. Index	
X	2. Labeling (check one) ☒ Draft Labeling ☐ Final Printed Labeling	Reviewer aid
X	3. Summary (21 CFR 314.50 (c))	
X	4. Chemistry section	
X	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)	
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)	
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)	
X	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)	
X	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)	
X	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))	
X	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)	Reviewer aid
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)	
X	10. Statistical section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)	
X	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)	e-media for Archive
X	12. Case reports forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)	e-media for Archive
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))	
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C 355 (b) (2) or (j) (2) (A))	
	15. Establishment description (21 CFR Part 600, if applicable)	
X	16. Debarment certification (FD&C Act 306 (k)(1))	
	17. Field copy certification (21 CFR 314.5 (k) (3))	
X	18. User Fee Cover Sheet (Form FDA 3397)	
	19. OTHER (Specify)	

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on reports in 21 CFR 314.80,314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
	( )

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Cover Letter - Both Paper & Electronic

Electronic Document Room

Guidance - Page 5

1. A PDF file of the cover letter named cover.pdf, which should include:

- *Appropriate regulatory information.*
- *A description of the submission.*
- *A description of which portions of the submission are presented only in paper, only in electronic format, or in both paper and electronic format.*
- *A description of the electronic submission including the contents of the media, their number and format, a description of the file types, and the total size of the submission (e.g., megabytes, gigabytes).*
- *Verification that the submission is virus free with a description of the software used to check the files for viruses.*
- *A description of any deviation from the specifications in this guidance document.*

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Cover Letter Example

We certify and agree to the following:

We have taken precautions to ensure that the data files are free of computer viruses and authorize CDER to use anti-virus software as appropriate.

We understand that the data (including any data media such as optical or magnetic disk) are an official part of the application and so may be retained indefinitely by the Agency as an archive of the application.

Any differences between the electronic data and the hard copy submission have been clearly defined. Other than the specifics identified, our electronic submission is identical in content to the hard copy.

2 Submission Format (Paper / Electronic)

Section	Description	Paper	Electronic
1	Index	☒	☐
2	Overall Summaries	☒	☐
3	Chemistry, Manufacturing & Controls	☒	☐
4	Samples and Labeling	☒	☐
5	Preclinical Pharmacology and Toxicology	☒	☐
6	Human Pharmacokinetics Section	☒	☐
8	Clinical Data Section	☒	☒
11	Case Report Tabulation Listings	☒	☐
12	Case Report Forms	☐	☒
13	Patent Information	☒	☐
14	Patent Certification	☒	☐
15	Bibliography	☒	☐

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Subsection 1.1

Electronic Document Room *NDA Table of Contents*

Paper and Electronic

- *Subsection 1.1: Index (NDA Table of Contents)*

This is one of a series of subsections being developed to facilitate the electronic submission of an NDA to CDER. Subsections are published independently as they are completed, but are intended for use with the other subsections in the series.

1. Regulatory reference

Section 314.50(b) states that the archival copy of an NDA, whether in paper or electronic format, is required to contain a comprehensive index to the summary, technical sections and supporting information contained in the submission. This index is commonly referred to as the NDA Table of Contents.

2. Organization of files

The comprehensive index should be provided as a single PDF file named ndatoc.pdf.

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NDATOC

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1.1 4. Table of contents

The NDA table of contents should be provided in the form of a PDF file and list all sections of the NDA. If a section is included as paper, the volumes and page numbers should be listed for that section. If the section is included in the electronic submission, the location of files should be listed by directory. For example, case report forms (CRFs) are in the CRF directory. In the same way that page numbers provide a user with a roadmap to a document, a hypertext link should be provided from the NDA table of contents to the corresponding table of contents for each subsection.

Current Guidance: Other Subsections

Electronic Document Room

- *Subsections 11 and 12 should be submitted to the EDR for Archiving*
- *No Other Subsections should be included in the electronic-media Archival copy at this time*

Submitting Archive Files
The EDR Staff Will . . .

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Document
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- ***Problem Resolution*** **-**

  The EDR Staff will

  – *Complete logs & technical data*

  – *Provide recommendations*

  The Project Manager will contact sponsors

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Rockville, Md. 20852-1833

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